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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/519,630	12/23/2004	Daisuke Machii	09859/0202256-US0	7855

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EXAMINER	
BALASUBRAMANIAN, VENKATARAMAN	
ART UNIT	**PAPER NUMBER**
1624	

MAIL DATE	DELIVERY MODE
05/03/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/519,630	MACHII ET AL.	
	Examiner	Art Unit	
	Venkataraman Balasubramanian	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1 and 8-12* is/are allowed.

6)☒ Claim(s) *2-7 and 13-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/23/2004, 3/28/2005, 5/8/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The preliminary amendment, which included cancellation of claims 21-24 and amendment to claims 8-20, filed on 2/23/2004, is made of record. Claims 1-20 are now pending.

Information Disclosure Statement

References cited in the Information Disclosure Statements dated 12/23/2004, 3/28/2005 and 5/8/2006, are made of record.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-7, 13-16 and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Recitation of " has the same meaning as defined above" in claim 2, 3 and 6 for R^5, R^6 and R^7 groups renders claims 2, 3, 6 and their dependent claims 4, 5 and 7 indefinite, as there is no definition of such groups in these claims. Proper linking of these variables to claim 1, on which these claims are dependent, is needed.

2. Claims 13, 14, 15 and 16 are indefinite as it is not clear whether these are compound claims or composition claims. If these are compound claims then they appear to be duplicate claims as there is no material difference between claim 1 and these claims. The attribute that a compound of a known structure has does not alter its structure in any way. See Intirtool, LTD. V. Texar Corp., 70 USPQ2D 1780. Note court

held that "In general, a claim preamble is limiting if recites essential structure or steps or if it is necessary to give" life, meaning, and vitality to claim.'.... However, if the body of the claim describes a structurally complete invention such that deletion of the preamble phrase does not effect the structure or steps of the claimed invention,' the preamble is generally not limiting unless there is clear reliance on the preamble during prosecution to distinguish the claimed invention from the prior art.""

Instant claim is a compound claim and is clearly defined by the structure of formula I namely an imidazopyrimidine core with a side chain bearing a amide group. Omission of the attributes to the compound of genus of claim 1 would not alter the structure of these compounds.

In addition, recitation of the term " comprise" in claims 13-16 renders these claims indefinite as the term is open-ended and can include more than what is being positively recited therein. See MPEP 2111.03 which states: The transitional term "comprising", which is synonymous with "including," "containing," or "characterized by," is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. See, e.g., Genentech, Inc. v. Chiron Corp., 112 F.3d 495, 501, 42 USPQ2d 1608, 1613 (Fed. Cir. 1997) ("Comprising" is a term of art used in claim language which means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claim.); Moleculon Research Corp. v. CBS, Inc., 793 F.2d 1261, 229 USPQ 805 (Fed. Cir. 1986); In re Baxter, 656 F.2d 679, 686, 210 USPQ 795, 803 (CCPA 1981); Ex parte Davis, 80 USPQ 448, 450 (Bd. App. 1948) ("comprising" leaves "the claim open for the inclusion of unspecified

ingredients even in major amounts"). Note if these claims are meant to be composition claims then they are duplicate of claim 12, as there appears to be no material difference between claim 12 and 13-16.

3. Claim 20 appears to be duplicate of claim 19 as the mode of action of the compound as insulin secretion promoter is relied on in both claims.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating diabetes, does not reasonably provide enablement for preventing diabetes and treating and preventing any or all diabetic complications generically embraced in the claim language. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Following apply.

The instant claims 17-20 are drawn to method of treating and or preventing diabetes and various complications of diabetes, based on the insulin secretion promoting activity and thereby reducing blood glucose levels by the instant compounds.

As recited, claims 17-20 are reach through claims. Reach through claims, in general have a format drawn to mechanistic, receptor binding or enzymatic functionality and thereby reach through any or all diseases, disorders or conditions for which they lack written description and enabling disclosure in the specification. In the instant case,

because of insulin secretion promoting activity by compound formula I, it is recited that instant compounds are useful for besides treatment, preventing of diabetes and preventing and treating of any or all complications of diabetes, for which there is no adequate written description and enabling disclosure in the instant specification. The scope of the claims includes treating and or preventing any or all disorders/ diseases due to diabetes by the mode of action of instant compounds namely insulin secretion promoting activity for which there is no enabling disclosure. The scope as recited would include Type I and Type 11 diabetes mellitus', diabetic complications, including, but not limited to, diabetic cataract, glaucoma, retinopathy, nephropathy (such as microaluminuria and progressive diabetic nephropathy), polyneuropathy, mononeuropathies, autonomic neuropathy, gangrene of the feet, atherosclerotic coronary arterial disease, peripheral arterial disease, nonketotic hyperglycemic-hyperosmolar coma, foot ulcers, joint problems, and a skin or mucous membrane complication (such as an infection, a shin spot, a Candida infection or necrobiosis lipoidica diabeticoruml; immune-complex vasculitis, and systemic lupus erythematosus (SLE), inflammatory disease of the heart, such as cardiomyopathy, ischemic heart disease hypercholesterolemia, and atherosclerosis; In addition, the scope of these claims include, besides treating, preventing of various diabetic complications. which are not adequately enabled solely based on the activity of the compounds provided in the specification. The instant compounds are disclosed to have insulin secretion promoting activity and it is recited that the instant compounds are therefore useful in treating any or all medical conditions stated above for which applicants provide no competent

evidence. It appears that the applicants are asserting that the embraced compounds because of their mode action as insulin secretion promoter shown in pages 239-246, that would be useful for all sorts of disorders and diseases. However, the applicants have not provided any competent evidence that the instantly disclosed tests are highly predictive for all the uses disclosed and embraced by the claim language for the intended host. Moreover, many if not most of neurological disorders are very difficult to treat despite the fact that there are many drugs with the analogous mode of action. There are several antidiabetic agents, which were known to reduce blood glucose due insulin secretion promoting activity, but none of them were found to prevent diabetes and or treat or prevent all complications of diabetes as embraced in the instant claims.

The term "to prevent" actually means to anticipate or counter in advance, to keep from happening etc. (as per Webster's II Dictionary) and there is no disclosure as to how one skilled in the art can reasonably establish the basis and the type of subject to which the instant compounds can be administered in order to have the "prevention" effect. There is no evidence of record, which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the disease(s) or disorder(s) claimed herein.

The scope of the claims involve more than four thousands of compounds of claim 1 as well as the thousand of diseases embraced by the term a diabetic complications.

No compound has ever been found to treat all types of medical conditions or diseases generally. Since this assertion is contrary to what is known in medicine, proof

must be provided that this revolutionary assertion has merits. The existence of such a "compound" is contrary to our present understanding of modern medicine.

Thus, it is beyond the skill of clinician today to get an agent to be effective in preventing diabetes, treating and preventing all complications of diabetes with a single agent generally. Note substantiation of utility and its scope is required when utility is "speculative", "sufficiently unusual" or not provided. See Ex parte Jovanovics, 211 USPQ 907, 909; In re Langer 183 USPQ 288. Also note Hoffman v. Klaus 9 USPQ 2d 1657 and Ex parte Powers 220 USPQ 925 regarding type of testing needed to support in vivo uses.

Next, applicant's attention is drawn to the Revised Utility and Written Description Guidelines, at 66 FR 1092-1099, 2001 wherein it is emphasized that 'a claimed invention must have a specific and substantial utility'. The disclosure in the instant case is not sufficient to enable the instantly claimed method treating and preventing solely based on the insulin secretion promoting activity disclosed for the compounds. The state of the art is indicative of the requirement for undue experimentation. See Schumann et al., PNAS, 104, 2861-2866, 2007.

In evaluating the enablement question, several factors are to be considered. Note In re Wands, 8 USPQ2d 1400 and Ex parte Forman, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1) The nature of the invention: Therapeutic use of the compounds in treating and/or preventing diseases based on the mode of action of instant compounds as insulin secretion promoting agents.

2) The state of the prior art: Recent publications expressed that the insulin secretion promoting activity effects are unpredictable and are still exploratory. See Schumann et al., cited above especially the concluding paragraph.

3) The predictability or lack thereof in the art: Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use for treating and preventing diabetes and any or all diabetic complications. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

4) The amount of direction or guidance present and 5) the presence or absence of working examples: Specification has no working examples to show preventing diabetes in general and treating and or preventing any or all diabetic complications. The state of the art is that the effects of insulin secretion promoters are unpredictable.

6) The breadth of the claims: The instant claims embrace thousands of compounds for preventing diabetes and treating and/or preventing any or all diabetic complications.

7) The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan, regarding the pharmaceutical use, for the reasons stated above.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims. In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of enzyme-inhibitor interactions in general, and the lack of working examples regarding the activity of the claimed compounds towards treating the variety of diseases of the instant claims, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

MPEP §2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was 'filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here and undue experimentation will be required to practice Applicants' invention.

Allowable Subject Matter

Claims 1 and 8-12, barring finding of any prior art in a subsequent search are allowed. Said claims would be allowable as prior art search in the related area did not teach or suggest the genus of compounds and composition embraced in the said claims.

Conclusion

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (571) 272-0662. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is James O. Wilson, whose telephone number is 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAG. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-2 17-9197 (toll-free).

Venkataraman Balasubramanian

4/29/2007